

Claims

5        1. Method for treatment of a condition associated with an elevated level of telomerase activity within a cell comprising the step of:

administering to said cell a therapeutically effective amount of an inhibitor of said telomerase activity.

10        2. Method for treatment of a condition associated with an increased rate of proliferation of a cell, comprising the step of:

15        administering to said cell a therapeutically effective amount of an agent active to reduce loss of telomere length within said cell during said proliferation.

20        3. Method for extending the ability of a cell to replicate, comprising the step of:

25        administering to said cell a replication extending amount of an agent active to reduce loss of telomere length within said cell during cellular replication.

30        4. A pharmaceutical composition comprising a therapeutically effective amount of an inhibitor of telomerase activity in a pharmaceutically acceptable buffer.

35        5. A pharmaceutical composition comprising a therapeutically effective amount of an agent active to reduce loss of telomere length within a cell during proliferation of said cell, in a pharmaceutically acceptable buffer.

6. Method for diagnosis of a condition in a patient associated with an elevated level of telomerase

activity within a cell, comprising the step of:

determining the presence or amount of telomerase within said cells in said patient.

5           7. Method for diagnosis of a condition associated with an increased rate of proliferation in a cell in an individual, comprising the steps of determining the length of telomeres within said cell.

10          8. Method for determining telomere length of an animal chromosome or group of chromosomes, said method comprising:

15          bringing together in a reaction mixture said chromosome(s) or telomere comprising fragment(s) thereof, a primer having at least two telomeric repeat units, and nucleoside triphosphates having the same nucleotides as the non-protruding strand of said telomere, wherein at least one of said nucleoside triphosphates or primer is labeled with a detectable label; and a DNA polymerase;

20          incubating said reaction mixture for sufficient time for said primer to be extended to provide a primer extended sequence;

25          separating said primer extended by size; and determining the size of said primer extended sequence by means of said label.

30          9. Method according to claim 8, wherein one of nucleoside triphosphates is labeled with a radioisotope and said size is determined by the level of radioactivity in relation to the amount of DNA present.

35          10. Method according to claim 8, wherein said nucleosides are combinations of A, T and C, or A, T and G.

11. Method of determining telomere length of an animal chromosome or group of chromosomes, said method

comprising:

fragmenting said chromosome(s) by a restriction endonuclease having a four base recognition site absent in the telomere sequence;

5 bringing together said fragments and a primer for said telomeric sequence, wherein said primer is labeled to allow for binding of said primer to a surface;

cross-linking said primer to said telomeric sequence;

10 isolating said telomeric sequence by means of said label; and

determining the size of said telomeric sequence bound to said surface.

15 12. Method according to claim 11, wherein said primer is conjugated with (1) an agent capable of cross-linking nucleic acids upon irradiation; and (2) a specific binding pair member; and said surface is conjugated with the complementary specific binding pair member.

20 25 13. Method according to claim 11, wherein said primer is conjugated with (1) an agent capable of cross-linking nucleic acids upon irradiation; and (2) a particle.

30 14. Method of reducing the rate of telomere shortening in a proliferating cellular composition, said method comprising:

introducing into cells of said cellular composition primers having from 2 to 3 repeats of the repeating unit of the cellular telomere.

35 15. Method of measuring the telomerase activity of a composition, said method comprising:

combining 1 or more repeats of the telomere unit sequence and nucleoside triphosphates lacking cytidine

5                   nucleotide, wherein at least one of said primer or nucleoside triphosphates is labeled with a detectable label, with the proviso that when said composition lacks a telomere sequence complementary to said probe, said telomere sequence is added to said composition;

incubating said composition for a predetermined time for said primer to be extended to provide an extended sequence; and

10                  determining the rate of formation of said extended sequence.

15                  16. Method according to claim 15, wherein one of said nucleoside triphosphates is labeled with a radioisotope, and said determining is by measuring radioactivity per unit weight of DNA.

20                  17. Method of inhibiting the proliferation of telomerase-comprising immortalized cells, said method comprising:

25                  contacting said immortalized cells with a telomerase inhibitor under conditions wherein said inhibitor enters said cells;

                        whereby said proliferation of said cells is inhibited.

25                  18. Method according to claim 17, wherein said inhibitor inhibits expression of telomerase.

30                  19. Method of according to claim 17, wherein said inhibition is an oligonucleotide sequence comprising the complementary sequence of the telomerase RNA.

35                  20. Method according to claim 17, wherein said oligonucleotide sequence is a ribozyme.

                        21. Method for extending the proliferative

capability of a mammalian cell population, said method comprising:

5 adding to said cells oligonucleotides comprising at least two repeats complementary to the sequence of the protruding strand of the telomere of the chromosomes of said cells, whereby the shortening of said telomere is slowed.

10 22. Method for treatment of a disease or condition associated with cell senescence, comprising the steps of:

15 administering a therapeutically effective amount of an agent active to derepress telomerase in the senescent cells.

15 23. Method for screening for a telomerase derepression agent, comprising the steps of:

20 contacting a potential agent with a cell lacking telomerase activity, and

25 determining whether said agent increases the level of said activity.

24. The method of claim 23, wherein said cell is a cell expressing an inducible T antigen.

25 25. The method of claim 1, wherein said cell is a fungal cell, and said administering reduces viability of said cell.

30 26. The method of claim 25, wherein said cell is a C. albicans cell.

35 27. Method for screening for agents useful in treatment of a human disease associated with an elevated level of telomerase activity in a human cell, comprising the step of testing potential said agents for activity in inhibiting telomerase activity.